UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,225	06/30/2003	David Hung	12.003011 DIV	1750

38732 7590 09/18/2007

CYTYC CORPORATION
250 CAMPUS DRIVE
MARLBOROUGH, MA 01752

EXAMINER	
SANG, HONG	
ART UNIT	**PAPER NUMBER**
1643	
MAIL DATE	**DELIVERY MODE**
09/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/608,225	HUNG ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,7 and 13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 7, and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Hung et al.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/20/2007 has been entered.

2. Claims 1-3, 5, 7, and 13-15 are pending. Claims 4, 6, 8-12, and 16-70 are cancelled. Claim 1 is amended.

3. Due to species election, claims are examined to the extent that the estrogen activity modulator is an estrogen antagonist.

4. The effective filing date for the claims 1-3, 5-7, and 13-15 is 5/17/1999 (see previous office action mailed on 9/6/06).

5. Applicant's amendment to the first line of specification to include the provisional application 60/117,281 is acknowledged.

Rejections Withdrawn

6. The rejection of claims 1-3, 9 and 13-15 under 35 U.S.C. 102(b) as being anticipated by Fabian et al. (J. Cell Biochem., 1993, 17G: 153-160, IDS) is withdrawn in view of applicant's amendments to the claims.

7. The rejection of claims 1-3, 5, 6, 8 and 13-15 under 35 U.S.C. 102(b) as being anticipated by Sauter et al. (British J. Cancer, 1997, 76(4): 494-501, IDS) is withdrawn in view of applicant's amendments to the claims.

8. The rejection of claims 1-3, 6-7 and 13-15 under 35 U.S.C. 102(b) as being anticipated by JAMA (JAMA, 1973, 224 (6): 823-827) is withdrawn in view of applicant's amendments to the claims.

9. The rejection of claims 1-3, 5-7 and 15 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9, 13, 15 and 19-21 of U.S. Patent No. 6,610,484B1 is withdrawn in view of applicant's amendment to the claims.

10. The rejection of claims 1, 6, 7, and 15 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 11, 13 and 22 of U.S. Patent No. 6,642,009B2 is withdrawn in view of applicant's amendment to the claims.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-3, 5, 7, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fabian et al. (J. Cell Biochem., 1993, 17G: 153-160, IDS), in view of Sauter et al. (British J. Cancer, 1997, 76(4): 494-501, IDS), JAMA (JAMA, 1973, 224 (6): 823-827), and Knight et al. (Ann. Clin. Res., 1980, 12(15): 202-207).

Fabian et al. teach a method of providing and cytologically examining ductal fluid obtained via fine needle aspiration from high and low risk of women, wherein high risk women include those with a first-degree relative with breast cancer, prior node-negative breast cancer, precancerous mastopathy (atypical hyperplasia or carcinoma in situ), and low-risk women include none of the above risk factors, nor a prior breast biopsy or clinical evidence of fibrocystic disease (see abstract). Fabian et al. teach that the needle was placed almost perpendicular to the chest wall and tissue behind nipple was probed deeply in an attempt to sample the terminal ducts (see page 154, 1st paragraph under METHODS). Fabian et al. teach that the ductal epithelial cells are examined cytologically and cancer markers including the estrogen receptor are determined (see page 154, right column). Fabian et al. teach that aspirates are classified cytologically as normal, apocrine metaplasia, epithelial hyperplasia, or dysplasia (see abstract, and

page 154, right column, 2nd paragraph). Fabian et al. teach that the difference in the prevalence of multiple biomarker abnormalities among various cytologic categories were statistically significant (p-0.02) (see abstract). Fabian et al. teach that the increased prevalence of single and multiple biomarker abnormalities with increase cytologic abnormalities indicates that one or more of these biological markers may be potentially useful in predicting who will be at highest risk for breast cancer development within a 5-10 year time frame (see last paragraph).

Fabian et al. do not teach obtaining the ductal epithelial cells by nipple aspiration of the milk ducts or by ductal lavage of at least one breast milk duct. Fabian et al. do not teach that providing the ductal fluid sample comprises receiving a sample which had been previously obtained. However, these deficiencies are made up for in the teachings of Sauter, JAMA reference, and Knight et al.

Sauter et al. teach a non-invasive method for early detection of breast cancer comprising collecting nipple aspirate fluid from a patient, cytologically analyzing the fluid (e.g. computerized image analysis of nipple aspirate fluid epithelial cells), and evaluating the promising cancer markers, wherein said patients were categorized by their risk for breast cancer as having no risk factors, a first degree relative with breast cancer, a history of curative treatment for ductal carcinoma in situ (DCIS), or invasive breast cancer, precancerous mastopathy (atypical hyperplasia (AH) or lobular carcinoma in situ (LCIS) or recently diagnosed invasive cancer of the breast (see abstract and page 495, left column, 2nd paragraph). Sauter et al. teach that the nipple aspirate fluid (NAF) was collected and transported to the cytology laboratory for

processing (see page 495, right column, 2nd paragraph), which meet the specific embodiment of claim 5). Sauter et al. teach that three of the slides were used for cytological examination, and each specimen was designated as containing scant, benign, atypical or malignant cells (see page 496, left column). Sauter et al. teach that the nipple aspirate fluid cytology correlated with increased breast cancer risk (P=0.002) (see abstract). Sauter et al. teach that biomarkers identified in nipple aspirate fluid may prove useful either as an adjunct to currently accepted breast cancer screening methods, or to evaluate response to a chemopreventive agent (see abstract).

The JAMA reference teaches a method for early detection of breast cancer in a patient comprising a) removing fluid through nipples with a suction device or by a method comprising inserting hair-like catheters into breast ducts with the help of an operating microscope, flushing the ducts with saline for cell studies; and b) examining the fluid to identify abnormal cells (see page 825, left column, 3rd and 4th paragraph, and page 826, right column, 3rd paragraph). The patients having abnormal cells include hyperplasia, chronic mastitis, intraductal papillomas, and severe dysplasia (the cells of these women could be considered pre-malignant), carcinomas including invasive carcinoma (see page 826, right column, 3rd and 4th paragraph). The patients that were diagnosed carcinoma appeared asymptomatic (see page 326, right column, 5th paragraph). JAMA reference teaches that the breast fluid from each duct is examined separately (see page 827, left column, 3rd paragraph). The JAMA reference teaches that women who are thought to be at high risk for breast cancer are examined this way every six month (see page 827, 4th paragraph). The JAMA reference teaches that the

fluids are tested for reverse transcriptase, an enzyme that has been implicated as a possible cancer marker (page 827, left column, 5th paragraph). The JAMA reference discloses using said method to study of breast fluid from patients without signs of breast disease, undetermined breast lesions, at high risk and with clinical evidence of breast cancer (see page 827, right column, last paragraph). While JAMA does not explicitly teach that the abnormal cells in the ductal fluid are epithelial cells, the abnormal cells in ductal fluid encompass exfoliated breast epithelial cells as evidenced by Sauter et al. Sauter et al. teach that the ductal fluid contains several types of cells, including exfoliated breast epithelial cells (see page 498, right column, 3rd paragraph).

Knight et al. teach that that estrogen receptor (ER) has now replaced clinical criteria in the selection of patients for endocrine therapy (such as Tamoxifen), and patients whose tumors do not contain ER should not be subjected to hormonal manipulation (see abstract). Knight et al. teach that in metastatic breast cancer, the absolute ER value may provide valuable information regarding endocrine responsiveness (see abstract). Knight et al. teach that ER measured on the primary tumor has been found to be an independent prognostic factor for both recurrence and survival (see abstract)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Fabian et al. to obtain ductal epithelial cells by nipple aspiration or ductal lavage of at least one breast milk duct as taught by Sauter or JAMA reference instead of by fine needle aspiration. One would have been motivated to do so because both nipple aspiration and ductal lavage are

non-invasive and can effectively obtain ductal epithelial cells as shown by Sauter and JAMA reference. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to obtain ductal epithelial cells by nipple aspiration or ductal lavage of breast milk duct because Sauter et al. teach nipple aspiration and JAMA reference teaches a method of obtain ductal cells by lavage of breast milk duct.

Moreover, it would have been *prima facie* obvious and one would have been motivated to use the estrogen receptor status obtained by Fabian to further provide information regarding the hormonal treatment (such as estrogen antagonist) response in view of the teachings of Knight. One of ordinary skill in the art would have a reasonable expectation of success to do so because Knight has shown that estrogen receptor can predict patient response to hormonal treatment.

13. Claims 1-3, 5, 7, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fabian et al. (J. Cell Biochem., 1993, 17G: 153-160, IDS), in view of Love (US Patent No. 6,221,622B1, Date of Patent: 4/24/2001, effective filing date: 4/28/1998), and Knight et al. (Ann. Clin. Res., 1980, 12(15): 202-207).

Fabian et al. teach a method of providing and cytologically examining ductal fluid obtained via fine needle aspiration from high and low risk of women, wherein high risk women include those with a first-degree relative with breast cancer, prior node-negative breast cancer, precancerous mastopathy (atypical hyperplasia or carcinoma in situ), and low-risk women include none of the above risk factors, nor a prior breast biopsy or clinical evidence of fibrocystic disease (see abstract). Fabian et al. teach that the

needle was placed almost perpendicular to the chest wall and tissue behind nipple was probed deeply in an attempt to sample the terminal ducts (see page 154, 1st paragraph under METHODS). Fabian et al. teach that the ductal epithelial cells are examined cytologically and cancer markers including the estrogen receptor are determined (see page 154, right column). Fabian et al. teach that aspirates are classified cytologically as normal, apocrine metaplasia, epithelial hyperplasia, or dysplasia (see abstract, and page 154, right column, 2nd paragraph). Fabian et al. teach that the difference in the prevalence of multiple biomarker abnormalities among various cytologic categories were statistically significant (p-0.02) (see abstract). Fabian et al. teach that the increased prevalence of single and multiple biomarker abnormalities with increase cytologic abnormalities indicates that one or more of these biological markers may be potentially useful in predicting who will be at highest risk for breast cancer development within a 5-10 year time frame (see last paragraph).

Fabian et al. do not teach obtaining the ductal epithelial cells by ductal lavage of single breast milk duct. Fabian et al. do not teach that providing the ductal fluid sample comprises receiving a sample which had been previously obtained. However, these deficiencies are made up for in the teachings of Love.

Love teaches a method of obtaining cellular, chemical and other materials from breast ducts, wherein a single milk duct is accessed and washed with a washing fluid to obtain marker materials from the lining duct, the washing fluid is then collected and the marker is analyzed (see abstract). Love teaches that such method permits reliable washing and retrieval of marker materials from an entire network of a sing milk duct to

enable screening, diagnosis, and monitoring of diseases associated with the lining of the milk duct, particularly for identifying cancer and pre-cancerous conditions (see column 3, lines 9-15). Love teaches that as the marker material are obtained entirely from a single ductal network, diagnosis can be made on a duct-by duct basis (see column 3, lines 15-18). Love teaches that the cellular marker materials may comprise epithelial cells from the lining of the duct, and non-cellular marker materials include proteins, peptides and other chemical species which may be secreted or otherwise released into a duct in response to a disease or other condition to be identified (see column 3, lines 35-47).

Knight et al. teach that that estrogen receptor (ER) has now replaced clinical criteria in the selection of patients for endocrine therapy (such as Tamoxifen), and patients whose tumors do not contain ER should not be subjected to hormonal manipulation (see abstract). Knight et al. teach that in metastatic breast cancer, the absolute ER value may provide valuable information regarding endocrine responsiveness (see abstract). Knight et al. teach that ER measured on the primary tumor has been found to be an independent prognostic factor for both recurrence and survival (see abstract)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Fabian et al. to obtain ductal epithelial cells by single ductal lavage as taught by Love instead of by fine needle aspiration. One would have been motivated to do so because single ductal lavage is non-invasive and can effectively retrieve useful cellular marker material (comprising

epithelial cells) from the lining of the duct. Moreover, Love teaches that as the marker material are obtained entirely from a single ductal network, diagnosis can be made on a duct-by duct basis (see column 3, lines 15-18). One of ordinary skill in the art would have a reasonable expectation of success to obtain ductal epithelial cells by single ductal lavage because Love teaches a method of obtain ductal fluid by single duct lavage.

It would have been *prima facie* obvious and one would have been motivated to use the estrogen receptor status obtained by Fabian to further provide information regarding the hormonal treatment (such as estrogen antagonist) response in view of the teachings of Knight. One of ordinary skill in the art would have a reasonable expectation of success to do so because Knight has shown that estrogen receptor can predict patient response to hormonal treatment.

While the references do not teach that the ductal sample was previously obtained, one skilled in the art would know that the sample can be analyzed immediately or stored properly for later analysis.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-3, 7 and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9, 13, 15 and 19-21 of U.S. Patent No. 6,610,484B1 in view of the teachings of Fabian et al. (J. Cell Biochem., 1993, 17G: 153-160, IDS), and Knight et al. (Ann. Clin. Res., 1980, 12(15): 202-207).

Claims 1 and 9 of U.S. Patent No. 6,610,484B1 is drawn to a method for identifying a patient having breast cancer or breast precancer, said method comprising: placing a ductal access tool comprising a single lumen in a breast duct of a patient, wherein the single lumen has an inner diameter large enough to retrieve clusters of greater than 10 cells; infusing a fluid into the duct through the single lumen, infusing a fluid into the duct through the single lumen; retrieving a ductal fluid sample from the accessed duct through the single lumen, wherein the ductal fluid sample comprises ductal epithelial cells and is free of ductal fluid from any other duct of the breast; and examining the ductal fluid sample to determine the presence of a marker comprising a protein, a polypeptide, a nucleic acid, a polynucleotide, an mRNA, a small organic molecule, a lipid, a fat, a glycoprotein, a glycopeptide, a carbohydrate, an oligosaccharide, a chromosomal abnormality, a whole cell having a marker molecule, a

particle, a secreted molecule, an intracellular molecule, and a complex of a plurality of molecules, wherein the method further comprising analyzing the cells in the ductal fluid sample for abnormal cytology. Claims 13, 15 and 19-21 of U.S. Patent No. 6,610,484B1 is drawn to a method of identifying a patient suspected of having breast cancer or breast precancer, said method comprising: examining a ductal fluid sample to determine the presence of a cancer or precancer marker comprising a protein, a polypeptide, a peptide, a nucleic acid, a polynucleotide, an mRNA, a small organic molecule, a lipid, a fat, a glycoprotein, a glycopeptide, a carbohydrate, an oligosaccharide, a chromosomal abnormality, a whole cell having a marker molecule, a particle, a secreted molecule, an intracellular molecule, and a complex of a plurality of molecules, wherein the fluid sample is obtained by a method comprising the steps of: (a) placing a ductal access tool comprising a single lumen in a breast duct of a patient, wherein the single lumen has an inner diameter large enough to retrieve clusters of greater than 10 cells; (b) infusing a fluid into the duct through the single lumen; and (c) retrieving the ductal fluid sample from the accessed duct through the single lumen, wherein the fluid sample comprises ductal epithelial cells and is free of ductal fluid from any other duct of the breast; wherein the presence of the marker in the ductal fluid sample identifies a cytological category selected from the group consisting of normal, abnormal, hyperplasia, atypical ductal carcinoma, ductal carcinoma in situ (DCIS), ductal carcinoma in situ--low grade (DCIS-LG), ductal carcinoma in situ--high grade DCIS-HG), invasive carcinoma, atypical mild changes, atypical marked changes, and atypical ductal hyperplasia (ADH), wherein the ductal fluid sample comprises ductal

epithelial cells, the cytological category is ductal carcinoma in situ--low grade (DCIS-LG), ductal carcinoma in situ--high grade (DCIS-HG), invasive carcinoma.

Claims 1, 9, 13, 15 and 19-21 of U.S. Patent No. 6,610,484B1 do not disclose the cancer marker to be detected is estrogen receptor. However, these deficiencies are made up for in the teachings of Fabian and Knight et al.

Fabian et al. teach a method of providing and cytologically examining ductal fluid obtained via fine needle aspiration from high and low risk of women (see abstract). Fabian et al. teach that the ductal epithelial cells are examined cytologically and cancer markers including the estrogen receptor are determined (see page 154, right column). Fabian et al. teach that the increased prevalence of single and multiple biomarker abnormalities with increase cytologic abnormalities indicates that one or more of these biological markers may be potentially useful in predicting who will be at highest risk for breast cancer development within a 5-10 year time frame (see last paragraph).

Knight et al. teach that that estrogen receptor (ER) has now replaced clinical criteria in the selection of patients for endocrine therapy (such as Tamoxifen), and patients whose tumors do not contain ER should not be subjected to hormonal manipulation (see abstract). Knight et al. teach that in metastatic breast cancer, the absolute ER value may provide valuable information regarding endocrine responsiveness (see abstract). Knight et al. teach that ER measured on the primary tumor has been found to be an independent prognostic factor for both recurrence and survival (see abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the claims 1, 9, 13, 15 and 19-21 of U.S. Patent No. 6,610,484B1 to detect estrogen receptor expressed by ductal epithelial cells in view of the teachings of Fabian and Knight. One would have been motivated to do so because Knight et al. teach that estrogen receptor is an independent prognosis marker for predicting recurrence, survival and treatment response. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to detect estrogen receptor expressed by ductal epithelial cells because Fabian has successfully detected estrogen receptor that are expressed by ductal epithelial cells.

It would have been *prima facie* obvious and one would have been motivated to further use the estrogen receptor status to provide information regarding hormonal treatment (such as estrogen antagonist) response in view of the teachings of Knight. One of ordinary skill in the art would have a reasonable expectation of success to do so because Knight has shown that estrogen receptor can predict patient response to hormonal treatment.

Claims 1-3, 7 and 15 are directed to an invention not patentably distinct from claims 1, 9, 13, 15 and 19-21 of commonly assigned U.S. Patent No. 6,610,484B1 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,610,484B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the

commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

16. Claims 1, 7, and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 11, 13 and 22 of U.S. Patent No. 6,642,009B2, in view of the teachings of Fabian et al. (J. Cell Biochem., 1993, 17G: 153-160, IDS), and Knight et al. (Ann. Clin. Res., 1980, 12(15): 202-207).

Claims 1, 2 and 11 of U.S. Patent No. 6,642,009B2 are drawn to a method to aid in diagnosing breast cancer or pre-cancer comprising: placing a ductal access tool comprising a single lumen in a breast duct of a patient, wherein the single lumen has an inner diameter large enough to retrieve clusters of greater than 10 cells; infusing a fluid into the duct through the single lumen; and retrieving a ductal fluid sample from the accessed duct through the single lumen, wherein the ductal fluid sample comprises ductal epithelial cells and is free of ductal fluid from any other duct of the breast,

wherein the method further comprising: examining the ductal fluid sample to determine the presence or absence of a marker, the method further comprising analyzing collected ductal epithelial cells by cytology. Claims 13 and 22 of U.S. Patent No. 6,642,009B2 are drawn to a method for analyzing breast markers or epithelial cells, comprising: placing a ductal access tool comprising a single lumen in a breast duct of a patient, wherein the single lumen has an inner diameter large enough to retrieve clusters of greater than 10 cells; infusing a fluid into the duct through the single lumen; retrieving a ductal fluid sample from the accessed duct through the single lumen, wherein the ductal fluid sample comprises ductal epithelial cells and is free of ductal fluid from any other duct of the breast; and determining the presence or absence of a marker in the ductal fluid sample, wherein the marker determined is cytology of ductal epithelial cells.

Claims 1, 2, 11, 13 and 22 of U.S. Patent No. 6,642,009B2 do not disclose the marker to be detected is estrogen receptor. However, these deficiencies are made up for in the teachings of Fabian and Knight et al.

Fabian et al. teach a method of providing and cytologically examining ductal fluid obtained via fine needle aspiration from high and low risk of women (see abstract). Fabian et al. teach that the ductal epithelial cells are examined cytologically and cancer markers including the estrogen receptor are determined (see page 154, right column). Fabian et al. teach that the difference in the prevalence of multiple biomarker abnormalities among various cytologic categories were statistically significant (p-0.02) (see abstract). Fabian et al. teach that the increased prevalence of single and multiple biomarker abnormalities with increase cytologic abnormalities indicates that one or

more of these biological markers may be potentially useful in predicting who will be at highest risk for breast cancer development within a 5-10 year time frame (see last paragraph).

Knight et al. teach that that estrogen receptor (ER) has now replaced clinical criteria in the selection of patients for endocrine therapy (such as Tamoxifen), and patients whose tumors do not contain ER should not be subjected to hormonal manipulation (see abstract). Knight et al. teach that in metastatic breast cancer, the absolute ER value may provide valuable information regarding endocrine responsiveness (see abstract). Knight et al. teach that ER measured on the primary tumor has been found to be an independent prognostic factor for both recurrence and survival (see abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the claims 1, 2, 11, 13 and 22 of U.S. Patent No. 6,642,009B2 to detect estrogen receptor expressed by ductal epithelial cells in view of the teachings of Fabian and Knight. One would have been motivated to do so because Knight et al. teach that estrogen receptor is an independent prognosis marker for predicting recurrence, survival and treatment response. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to detect estrogen receptor expressed by ductal epithelial cells because Fabian has successfully detected estrogen receptor that are expressed by ductal epithelial cells.

It would have been *prima facie* obvious and one would have been motivated to further use the estrogen receptor status to provide information regarding hormonal

treatment (such as estrogen antagonist) response in view of the teachings of Knight. One of ordinary skill in the art would have a reasonable expectation of success to do so because Knight has shown that estrogen receptor can predict patient response to hormonal treatment.

Claims 1, 7, and 15 are directed to an invention not patentably distinct from 1, 2, 11, 13 and 22 of commonly assigned U.S. Patent No. 6,642,009B2 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,642,009B2, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
Sept. 5, 2007

/Christopher Yaen/
Primary Examiner
Art Unit 1643
September 13, 2007